MORRISON & FOERSTER LLP

Attorneys at Law
3811 Valley Centre Drive, Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5100
Facsimile: (858) 720-5125

OFFICIAL

To: **U.S. Patent and Trademark Office** **Facsimile: 703 872-9306**
Mail Stop Amendment

From: Gregory P. Einhorn, Esq. **Date: June 15, 2004**

We are transmitting a total of 4 pages (including this page).
Original or hard copy to follow if this box is checked ☐.

If you do not receive all pages, please call 858 720-7937 as soon as possible.

Preparer of this slip has confirmed that facsimile number given is correct:

Comments:

Attorney Docket:	56446-2000312
Group Art Unit:	1652
Examiner:	D. Ramirez
Serial No.:	09/619,032
Filing Date:	July 19, 2000
Inventor(s):	Dennis MURPHY
Title:	ALPHA-GALACTOSIDASES AND METHODS OF USING THEM (AMENDED)
	Papers attached:

1. Declaration Under 37 C.F.R. 1.132 (signed) (3 pages)
(Original (unsigned) submission by fax on 6/4/04)

sd-204507

Attorney's Docket No.: 56446-20003.12/-004004 / D1120-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Murphy, et al. Art Unit : 1652
Serial No. : 09/619,032 Examiner : Delia M. Ramirez, Ph.D.
Filed : July 19, 2000
Title : ALPHA-GALACTOSIDASES AND METHODS OF USING THEM (amended)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

OFFICIAL

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, Jay Short, am a co-inventor with Dennis Murphy, John Reid and Eric J. Mathur, on the above-identified patent application.

2. I am an expert in the field of molecular biology and enzyme development and was an expert at the time of the invention. I am presently employed as CEO and as a research scientist at Diversa Corporation, San Diego, CA, assignee of the above-referenced patent application. My resume is attached as documentation of my credentials.

3. I declare that procedures for making alpha galactosidase fragments and sequence variations, e.g., with substitutions, deletions, insertions, and additions, were routine in the art at the time of the invention. Procedures for identifying alpha galactosidase fragments and variants were conventional and routine in the art at the time of the invention. Procedures for identifying polypeptides having alpha galactosidase activity were conventional and routine in the art at the time of the invention. For example, an assay for identifying polypeptide having alpha galactosidase activity described in the specification in Example 2, on pages 18 to 19. One of ordinary skill in the art using the teaching of the specification could have made and expressed ____.

nucleic acids encoding alpha galactosidases having a percent sequence identity to the exemplary SEQ ID NO:4, or, which hybridized under defined conditions to the exemplary SEQ ID NO:4, and using routine screening could have determined with predicable positive results which of those nucleic acids encoded a polypeptide having alpha galactosidase activity. Accordingly, using the teaching of the specification one of ordinary skill in the art would have been able to ascertain the scope of the genus of alpha galactosidases used in the claimed methods with reasonable clarity and recognized that Applicants' were in possession of the claimed invention at the time of filing.

4. I declare that the art at the time of the invention and the level of skill of the person of ordinary skill in the art for screening enzymes for alpha galactosidase activity was very high. It would not have been necessary for the skilled artisan to understand which regions of the α-galactosidases used in the claimed methods could be modified to gain a function or activity, or, modified without loss of a function or activity. It would not have been necessary for the skilled artisan to understand which specific regions of α-galactosidase sequence or structure needed to be modified without affecting function or activity to routinely generate the genus of polypeptides used in the claimed methods. Methods for making and screening sequence modifications and enzyme fragments were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate α-galactosidase-encoding sequences without need of knowing which specific regions of a sequence or structure affected function or activity. Methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (α-galactosidase) screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. At the time of the invention, high through-put *in vivo* (e.g., whole cell) nucleic acid expression and enzyme (α-galactosidase) screening protocols were well known in the art. The specification sets forth an exemplary α-galactosidase screening assay to determine if a polypeptide is within the scope of the genus used in the claimed methods (see, e.g., Example 2, of the specification). Using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of α-galactosidase structure needed to be modified to generate

a genus of nucleic acids or polypeptides for practicing the invention without undue experimentation. The specification presented to the skilled artisan a rational and predictable scheme for making the genus of α-galactosidases and α-galactosidase-encoding sequences, including a rational and predictable scheme for modifying the exemplary SEQ ID NO:4 with an expectation of obtaining a desired (e.g., new or modified or the same) function. The specification provided sufficient guidance to one of ordinary skill in the art to make and use the genus of polypeptides to practice the methods of the invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date: 6/14/04

Jay Short